

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Norbert O. Reich et al. Docket No.: 30794.30USD1
Filed: December 7, 2001
Title: MODULATORS OF DNA CYTOSINE-5 METHYLTRANSFERASE AND
METHODS FOR USE THEREOF

CERTIFICATE OF MAILING OR TRANSMISSION UNDER 37 CFR 1.10

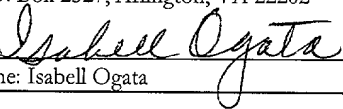
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0327.

By:

Name: Isabell Ogata



PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
U.S. Patent and Trademark Office
P. O. Box 2327
Arlington, Virginia 22202-0327

Dear Sir:

Prior to a first Office Action, please amend the above-identified application as
follows.

IN THE SPECIFICATION

On page 1, please insert the following sentence before the first line:

This application is a Division of application Serial No. 09/485,071, filed
February 3, 2000, entitled MODULATORS OF DNA CYTOSINE-5
METHYLTRANSFERASE AND METHODS FOR USE THEREOF, which application
is incorporated herein by reference.

IN THE CLAIMS

Please cancel claims 1-20 and add new claims 21-35 as follows:

21. A method of inhibiting methylation of DNA comprising contacting a DCMTase with a synthetic inhibitor molecule so as to form an enzyme/synthetic inhibitor molecule complex in the presence of the DNA, wherein the synthetic inhibitor molecule comprises a C-5 methylcytosine which recognizes and binds an allosteric site on DCMTase, thereby inhibiting DNA methyltransferase activity.

22. A method of inhibiting proliferation of cancer cells comprising administering to a subject a synthetic inhibitor molecule which recognizes and binds an allosteric site on DCMTase thereby resulting in an enzyme/synthetic inhibitor molecule complex, the presence of the complex inhibiting DCMTase-mediated methylation of DNA, thereby inhibiting proliferation of the cancer cells.

23. The method of claim 22, wherein the cancer cell is from lung, breast, prostate, pancreas or colon.

24. The method of claim 21, wherein the synthetic inhibitor molecule is a synthetic oligonucleotide comprising a C-5 methylcytosine and which recognizes and binds an allosteric site on DNA cytosine methyltransferase (DCMTase) thereby modulating DCMTase activity associated with the allosteric site.

25. The method of claim 22, wherein the subject is a human.

26. The method of claim 22, wherein the subject is an animal.

27. The method of claim 26, wherein the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine or canine.

28. A method of identifying a molecule which recognizes and binds an allosteric site on DCMTase comprising:

- (a) contacting a molecule with DCMTase in the presence of DNA and AdoMet;
- (b) measuring DCMTase activity, an increase or decrease in DCMTase activity being indicative of a modulator of DCMTase; and

- (c) determining whether the modulation of DCMTase activity is via binding an allosteric site on DCMTase.
29. The method of claim 28, wherein the modulator is an inhibitor.
30. The method of claim 28, wherein DCMTase activity is measured using a steady-state assay.
31. The method of claim 22, wherein the synthetic inhibitor molecule comprises a C-5 methylcytosine.
32. The method of claim 22, wherein the synthetic inhibitor molecule is a synthetic oligonucleotide comprising a C-5 methylcytosine and which recognizes and binds an allosteric site on DNA cytosine methyltransferase (DCMTase) thereby modulating DCMTase activity associated with the allosteric site.
33. The method of claim 24, wherein the subject is a human.
34. The method of claim 24, wherein the subject is an animal.
35. The method of claim 34, wherein the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine or canine.

REMARKS

Prior to a first Office Action in this application, Applicants request that original claims 1-20 be cancelled and new claims 21-35 be added.

It is submitted that this application is now in good order for allowance and such allowance is respectively solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

Norbert O. Reich et al.

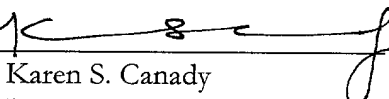
By their attorneys,

GATES & COOPER LLP

6701 Center Drive West, Suite 1050
Los Angeles, California 90045
(310) 641-8797

Date: December 7, 2001

KSC/io

By: 
Karen S. Canady
Reg. No.: 39,927